Complete Summary

GUIDELINE TITLE

(1) Smallpox as a biological weapon: medical and public health management. (2) Smallpox as a biological weapon. (Addendum)

BIBLIOGRAPHIC SOURCE(S)

Henderson DA, Inglesby TV, Bartlett JG, Ascher MS, Eitzen E, Jahrling PB, Hauer J, Layton M, McDade J, Osterholm MT, O'Toole T, Parker G, Perl T, Russell PK, Tonat K. Smallpox as a biological weapon: medical and public health management. Working Group on Civilian Biodefense. JAMA 1999 Jun 9;281(22):2127-37. [51 references] PubMed

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GUIDELINE STATUS

This is the current release of the guideline.

* * REGULATORY ALERT * *

FDA WARNING/REGULATORY ALERT

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory information has been released.

On November 10, 2005, the U.S. Food and Drug Administration (FDA) notified physicians, nurses, medical technologists, pharmacists and other healthcare professionals of the potential for life-threatening falsely elevated glucose readings in patients who have received parenteral products containing maltose or galactose, or oral xylose, and are subsequently tested using glucose dehydrogenase pyrroloquinolinequinone (GDH-PQQ) based glucose monitoring systems. There have been reports of the inappropriate administration of insulin and consequent life-threatening/fatal hypoglycemia in response to erroneous test results obtained from patients receiving parenteral products containing maltose. Cases of true hypoglycemia can go untreated if the hypoglycemic state is masked by false elevation of glucose readings. A preliminary listing of U.S. products that may cause glucose test interference is provided. See the FDA Web site for more information.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Exposure to or infection with smallpox

GUIDELINE CATEGORY

Diagnosis
Evaluation
Management
Treatment

CLINICAL SPECIALTY

Emergency Medicine
Family Practice
Infectious Diseases
Internal Medicine
Obstetrics and Gynecology
Pathology
Pediatrics
Preventive Medicine

INTENDED USERS

Advanced Practice Nurses
Allied Health Personnel
Clinical Laboratory Personnel
Hospitals
Nurses
Physician Assistants
Physicians
Public Health Departments

GUIDELINE OBJECTIVE(S)

To develop consensus-based recommendations for measures to be taken by medical and public health professionals following the use of smallpox as a biological weapon against a civilian population

TARGET POPULATION

Adults, pregnant women, children, and immunosuppressed persons exposed to or infected with smallpox as a biological weapon

INTERVENTIONS AND PRACTICES CONSIDERED

Diagnosis

1. Assessment of clinical and epidemiological features
2. Laboratory confirmation of vesicular or pustular fluid by electron microscopic examination
3. Immediate notification of state or local health department laboratories regarding the shipping of specimens

Postexposure Therapy

1. Supportive therapy
2. Antibiotics as indicated for treatment of occasional secondary bacterial infections

   Note: The therapeutic benefits of medications for smallpox patients (thiosemicarbazones, cytosine arabinoside, adenine arabinoside, rifampicin and cidofovir) are discussed but not recommended.

Postexposure Public Health Infection Control/Management

1. Smallpox vaccine administration of smallpox patients and their close contacts
2. Isolation of smallpox patients
3. Surveillance measures focused on those at greatest risk
4. An emergency vaccination program that would include all health care workers at clinics or hospitals that might receive patients; all other essential disaster response personnel, such as police, firefighters, transit workers, public health staff, and emergency management staff who might come into contact with patients; and mortuary staff who might have to handle bodies
5. Possible governmental level quarantine
6. Selected use of vaccinia immune globulin (VIG)

Postexposure Hospital Epidemiology and Infection Control

1. Vaccination of all hospital employees and patients
2. Selected use of vaccinia immune globulin
3. Isolation of patients to rooms that are under negative pressure and equipped with high-efficiency particulate air filtration
4. Designation of specific hospitals or facilities for smallpox care, as warranted

5. Standard precautions using gloves, gowns, and masks, and placement of laundry and waste in biohazard bags and autoclaved before being laundered or incinerated
6. Laboratory examination in high-containment (biological safety level-4) facilities and designated laboratories with the appropriate trained personnel and equipment

Decontamination

MAJOR OUTCOMES CONSIDERED

- Efficacy of management strategies (e.g., smallpox vaccinations, infection control measures) in preventing smallpox or minimizing severity of disease or outbreaks
- Complications of smallpox vaccine administration

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases
Searches of Unpublished Data

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Not applicable

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Expert Consensus

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not applicable

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not applicable

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

The first draft of the consensus statement was a synthesis of information obtained in the evidence-gathering process. Members of the working group provided formal written comments that were incorporated into the second draft of the statement. The working group reviewed the second draft on October 30, 1998. No significant disagreements existed and comments were incorporated into a third draft. The fourth and final statement incorporates all relevant evidence obtained by the literature search in conjunction with final consensus recommendations supported by all working group members.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Not stated

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Diagnosis

The discovery of a single suspected case of smallpox must be treated as an international health emergency and be brought immediately to the attention of national officials through local and state health authorities.

The majority of smallpox cases present with a characteristic rash that is centrifugal in distribution, ie, most dense on the face and extremities. The lesions appear during a 1- to 2-day period and evolve at the same rate. On any given part of the body, they are generally at the same stage of development. In varicella (chickenpox), the disease most frequently confused with smallpox, new lesions appear in crops every few days and lesions at very different stages of maturation (i.e., vesicles, pustules, and scabs) are found in adjacent areas of skin

(see Figure 3 in the original guideline document). Varicella lesions are much more superficial and are almost never found on the palms and soles. The distribution of varicella lesions is centripetal, with a greater concentration of lesions on the trunk than on the face and extremities.

The signs and symptoms of both hemorrhagic and malignant smallpox were such that smallpox was seldom suspected until more typical cases were seen and it was recognized that a smallpox outbreak was in progress. Hemorrhagic cases were most often initially identified as meningococcemia or severe acute leukemia. Malignant cases likewise posed diagnostic problems, most often being mistaken for hemorrhagic chickenpox or prompting surgery because of severe abdominal pain.

Laboratory confirmation of the diagnosis in a smallpox outbreak is important. Specimens should be collected by someone who has recently been vaccinated (or is vaccinated within 1 or 2 days) and who wears gloves and a mask. To obtain vesicular or pustular fluid, it is often necessary to open lesions with the blunt edge of a scalpel. The fluid can then be harvested on a cotton swab. Scabs can be picked off with forceps. Specimens should be deposited in a screw-capped plastic tube that should be sealed with adhesive tape at the juncture of stopper and tube. This tube, in turn, should be enclosed in a second durable, watertight container. State or local health department laboratories should immediately be contacted regarding the shipping of specimens. Laboratory examination requires high-containment (biological safety level-4) facilities and should be undertaken only in designated laboratories with the appropriate training and equipment. Once it is established that the epidemic is caused by smallpox virus, clinically typical cases would not require further laboratory confirmation.

Smallpox infection can be rapidly confirmed in the laboratory by electron microscopic examination of vesicular or pustular fluid or scabs. Although all orthopoxviruses exhibit identically appearing brick-shaped virions, history taking and clinical picture readily identify cowpox and vaccinia. Although smallpox and monkeypox virions may be indistinguishable, naturally occurring monkeypox is found only in tropical rain forest areas of Africa. Definitive laboratory identification and characterization of the virus involves growth of the virus in cell culture or on chorioallantoic egg membrane and characterization of strains by use of various biologic assays, including polymerase chain reaction techniques and restriction fragment-length polymorphisms. The latter studies can be completed within a few hours.

Preexposure Preventive Vaccination

Before 1972, smallpox vaccination was recommended for all United States children at age 1 year. Most states required that each child be vaccinated before school entry. The only other requirement for vaccination was for military recruits and tourists visiting foreign countries. Most countries required that the individual be successfully vaccinated within a 3-year period prior to entering the country. Routine vaccination in the United States stopped in 1972 and since then, few persons younger than 30 years have been vaccinated. Those under 30 years now account for about 45% of the US population.

The immune status of those who were vaccinated more than 30 years ago is not clear. The duration of immunity, based on the experience of naturally exposed susceptible persons, has never been satisfactorily measured. Neutralizing antibodies are reported to reflect levels of protection, although this has not been validated in the field. These antibodies have been shown to decline markedly during a 10- to 20-year period. Thus, a substantial proportion of those who received the recommended single-dose vaccination as children do not have lifelong immunity. However, among a group who had been vaccinated at birth and at ages 8 and 18 years as part of a study, neutralizing antibody levels remained stable during a 30-year period. It is possible, therefore, that those vaccinated successfully on 2 or more occasions may have residual antibody. However, comparatively few persons today have been successfully vaccinated on more than 1 occasion.

It is to be noted that in endemic countries, estimates of vaccine efficacy after primary vaccination have been found to be 90% or higher among adults who were vaccinated only as children. This undoubtedly reflects the fact that inapparent smallpox infections have occurred among vaccinated contacts with a concomitant significant rise in antibody titer. Since naturally occurring smallpox infections result in lifetime immunity, the apparent high level of efficacy of primary vaccination alone, based on experience in endemic areas, is misleading.

At present, the supplies of vaccine worldwide are limited, but actions are being taken to improve the availability of vaccine in case of need. As of late 2001, the United States (US) has an amount of vaccine that, with appropriate dilution, was sufficient to vaccinate 50 million persons. This quantity is based on recently published studies that demonstrated that the US smallpox vaccine currently in reserve (Dryvax, Wyeth Laboratories, Marietta, Pa) could be safely diluted to a 1:5 dilution without reducing the rate of successful vaccination. The smallpox vaccine was produced in the 1970s by growth of vaccinia virus (New York Board of Health strain) on the scarified skin of calves. Production has begun to produce the same strain of vaccinia virus in tissue cell cultures (some in MRC-5 cells and some in Vero cells) with the expectation that a total of 280 million doses of vaccine would be available by late 2002.

A World Health Organization (WHO) survey of other countries reveals that, in total, they have in stock between 50 and 100 million doses, not all of which is thought to meet international standards for potency and stability. Several countries have indicated that they expect to augment their vaccine reserves either by production in national laboratories or through purchase.

Because of the small amounts of vaccine available, a preventive vaccination program to protect individuals such as emergency and health care personnel is not an option at this time. When additional supplies of vaccine are procured, a decision to undertake preventive vaccination of some portion of the population will have to weigh the relative risk of vaccination complications against the threat of contracting smallpox.

Before extensive vaccination can be undertaken, adequate supplies of vaccinia immune globulin (VIG) for use in the treatment of progressive vaccinia and severe cutaneous reactions occurring as a complication of vaccination must be available. Such supplies are now being procured for the United States.

Postexposure Therapy

At this time, the best that can be offered to the patient infected with smallpox is supportive therapy plus antibiotics as indicated for treatment of occasional secondary bacterial infections. No antiviral substances have yet proved effective for the treatment of smallpox. Initial reports in the 1960s described the therapeutic benefits of the thiosemicarbazones, cytosine arabinoside, adenine arabinoside, and rifampicin, but ultimately they proved to be ineffective.

Recent studies in tissue culture, mice, and a small number of monkeys have suggested the possibility that cidofovir, a nucleoside analog DNA polymerase inhibitor, might prove useful in preventing smallpox infection if administered within 1 or 2 days after exposure. At this time, there is no evidence to suggest that cidofovir would be effective in the treatment of smallpox once symptoms had appeared. Moreover, the potential utility of this drug would be of limited value in an epidemic, given the fact that it must be administered intravenously and its use is sometimes accompanied by serious renal toxicity.

Postexposure Infection Control

A smallpox outbreak poses difficult public health problems because of the ability of the virus to continue to spread throughout the population unless checked by vaccination and/or isolation of patients and their close contacts.

A clandestine aerosol release of smallpox, even if it infected only 50 to 100 persons to produce the first generation of cases, would rapidly spread in a now highly susceptible population, expanding with each generation of cases, by a factor of 10 times or more during the winter and spring months when seasonal transmission is highest. Between the time of an aerosol release of smallpox virus and diagnosis of the first cases, an interval as long as 2 weeks or more is apt to occur because of the average incubation period of 12 to 14 days and the lapse of several additional days before a rash was sufficiently distinct to suggest the diagnosis of smallpox. By that time, there would be no risk of further environmental exposure from the original aerosol release because the virus is fully inactivated within 2 days. However, close contacts of the first wave of cases would already have been infected and would be incubating the disease.

As soon as the diagnosis of smallpox is made, all individuals in whom smallpox is suspected should be isolated immediately and all household and other face-to-face contacts should be vaccinated and placed under surveillance. It is important that discretion be used in identifying contacts of patients to ensure, to the extent that is possible, that vaccination and adequate surveillance measures are focused on those at greatest risk. Specifically, it is recommended that contacts be defined as persons who have been in the same household as the infected individual or who have been in face-to-face contact with the patient after the onset of fever. Household members of those in face-to-face contact should also be vaccinated. Experience during the smallpox global eradication program showed that patients did not transmit infection until after the prodromal fever had given way to the rash stage of illness. An emergency vaccination program is also indicated that would include all health care workers at clinics or hospitals that might receive patients; all other essential disaster response personnel, such as police, firefighters, transit workers, public health staff, and emergency management staff

who might come into contact with patients; and mortuary staff who might have to handle bodies. The working group recommends that all such personnel for whom vaccination is not contraindicated should be vaccinated immediately irrespective of prior vaccination status.

Vaccination administered within 4 days of first exposure has been shown to offer some protection against acquiring infection and significant protection against a fatal outcome. Those who have been vaccinated at some time in the past will normally exhibit an accelerated immune response. Thus, it would be prudent, when possible, to assign those who had been previously vaccinated and just revaccinated to duties involving close patient contact.

Because the widespread dissemination of smallpox virus by aerosol poses a serious threat in hospitals, patients should be isolated in the home or other nonhospital facility whenever possible. Home care for most patients is a reasonable approach, given the fact that little can be done for a patient other than to offer supportive therapy. Isolation of all contacts of exposed patients would be logistically difficult and, in practice, should not be necessary. Because contacts, even if infected, are not contagious until onset of rash, a practical strategy calls for all contacts to have temperatures checked at least once each day, preferably in the evening. Any increase in temperature higher than 38Â°C (101Â°F) during the 17-day period following last exposure to the case would suggest the possible development of smallpox and be cause for isolating the patient immediately, preferably at home, until it could be determined whether the contact had smallpox. All close contacts of the patients should be promptly vaccinated.

Although cooperation by most patients and contacts in observing isolation could be ensured through counseling and persuasion, there may be some for whom forcible quarantine will be required. Some states and cities in the United States, but not all, confer broad discretionary powers on health authorities to ensure the safety of the public's health and, at one time, this included powers to quarantine. Under epidemic circumstances, this could be an important power to have. Thus, each state and city should review its statutes as part of its preparedness activities.

During the smallpox epidemics in the 1960s and 1970s in Europe, there was public alarm whenever outbreaks occurred and, sometimes, a demand for mass vaccination over a wide area, even when the vaccination coverage of the population was high. In the United States, where few people now have protective levels of immunity, similar levels of concern must be anticipated. However, until there is an adequate global vaccine supply, the vaccine has to be carefully conserved and a major emphasis placed on the rapid isolation of smallpox patients.

Hospital Epidemiology and Infection Control

The working group recommends that in an outbreak setting, all hospital employees as well as patients in the hospital be vaccinated. For individuals who are immunocompromised or for whom vaccination is otherwise contraindicated, vaccinia immune globulin should be provided, if available. If it is not available, a judgment will have to be made regarding the relative risks of acquiring the disease in contrast with the risks associated with vaccination.

In the event of a limited outbreak with few cases, patients should be admitted to the hospital and confined to rooms that are under negative pressure and equipped with high-efficiency particulate air filtration. In larger outbreaks, home isolation and care should be the objective for most patients. However, not all will be able to be so accommodated and, to limit nosocomial infections, authorities should consider the possibility of designating a specific hospital or hospitals for smallpox care. All persons isolated as such and those caring for them should be immediately vaccinated. Employees for whom vaccination is contraindicated should be furloughed.

Standard precautions using gloves, gowns, and masks should be observed. All laundry and waste should be placed in biohazard bags and autoclaved before being laundered or incinerated. A special protocol should be developed for decontaminating rooms after they are vacated by patients (see "Decontamination" section).

Laboratory examination requires high-containment (biological safety level-4) facilities and should be undertaken only in designated laboratories with the appropriate trained personnel and equipment. Specific recommendations for safe specimen transport are described in the original guideline document section on "Diagnosis."

Protecting against the explosive spread of virus from the hemorrhagic or malignant case is difficult. Such cases occurring during the course of an outbreak may be detected if staff is alert to the possibility that any severe, acute, prostrating illness must be considered smallpox until proven otherwise.

Vaccine Administration and Complications

Smallpox vaccine is currently approved by the US Food and Drug Administration (FDA) for use only in persons in special-risk categories, including laboratory workers directly involved with smallpox or closely related orthopoxviruses. Under epidemic circumstances, widespread vaccination would be indicated, as recommended by the working group.

Vaccination has been successfully and safely administered to persons of all ages, from birth onward. However, there are certain groups for whom elective vaccination has not been recommended because of the risk of complications. Under epidemic circumstances, however, such contraindications will have to be weighed against the grave risks posed by smallpox. If available, vaccinia immune globulin can be administered concomitantly with vaccination to minimize the risk of complications in these persons.

Vaccination is normally performed using the bifurcated needle (see Figure 4 in the original guideline document). A sterile needle is inserted into an ampoule of reconstituted vaccine and, on withdrawal, a droplet of vaccine sufficient for vaccination is held by capillarity between the 2 tines. The needle is held at right angles to the skin; the wrist of the vaccinator rests against the arm. Fifteen perpendicular strokes of the needle are rapidly made in an area of about 5 mm in diameter. The strokes should be sufficiently vigorous so that a trace of blood appears at the vaccination site after 15 to 30 seconds. After vaccination, excess vaccine should be wiped from the site with gauze that should be discarded in a

hazardous waste receptacle. The site should be covered with a loose, nonocclusive bandage to deter the individual from touching the site and perhaps transferring virus to other parts of the body.

After about 3 days, a red papule appears at the vaccination site and becomes vesicular on about the fifth day (see Figure 5 in the original guideline document). By the seventh day, it becomes the typical Jennerian pustule, umbilicated, multilocular, containing turbid lymph and surrounded by an erythematous areola that may continue to expand for 3 more days. Regional lymphadenopathy and fever is not uncommon. As many as 70% of children have 1 or more days of temperature higher than 39Â°C (100Â°F) between days 4 and 14. The pustule gradually dries, leaving a dark crust, which normally falls off after about 3 weeks.

A successful vaccination for those with partial immunity may manifest a gradient of responses. These range from what appears to be a primary take (as described herein) to an accelerated reaction in which there may be little more than a papule surrounded by erythema that reaches a peak between 3 and 7 days. A response that reaches a peak in erythema within 48 hours represents a hypersensitivity reaction and does not signify that growth of the vaccinia virus has occurred. Persons exhibiting such a reaction should be revaccinated.

Complications

The frequency of complications associated with use of the New York Board of Health strain (the strain used throughout the United States and Canada for vaccine) is the lowest for any established vaccinia virus strain, but the risks are not inconsequential. Data on complications gathered by the Centers for Disease Control and Prevention (CDC) in 1968 are shown in Table 1 in the original guideline document and are discussed in the "Potential Harms" section of this summary. Complications occurred most frequently among primary vaccinees.

Groups at Special Risk for Complications

Consensus recommendations for special-risk groups as set forth herein reflect the best clinical and science-based judgment of the working group and do not necessarily correspond to US Food and Drug Administration-approved uses.

Five groups of persons are ordinarily considered at special risk of smallpox vaccine complications: (1) persons with eczema or other significant exfoliative skin conditions; (2) patients with leukemia, lymphoma, or generalized malignancy who are receiving therapy with alkylating agents, antimetabolites, radiation, or large doses of corticosteroids; (3) patients with human immunodeficiency virus (HIV) infection; (4) persons with hereditary immune deficiency disorders; and (5) pregnant women. If persons with contraindications have been in close contact with a smallpox patient or the individual is at risk for occupational reasons, vaccinia immune globulin (VIG), if available, may be given simultaneously with vaccination in a dose of 0.3 mL/kg of body weight to prevent complications. This does not alter vaccine efficacy. If VIG is not available, vaccine administration may still be warranted, given the far higher risk of an adverse outcome from smallpox infection than from vaccination.

Vaccinia Immune Globulin (VIG) Therapy for Complications

Vaccinia immune globulin is valuable in treating patients with progressive vaccinia, eczema vaccinatum, severe generalized vaccinia, and periocular infections resulting from inadvertent inoculation. It is administered intramuscularly in a dose of 0.6 mL/kg of body weight. Because the dose is large (e.g., 42 mL for a person weighing 70 kg), the product is given intramuscularly in divided doses over a 24- to 36-hour period and may be repeated, if necessary, after 2 to 3 days if improvement is not occurring. Because the availability of VIG is so limited, its use should be reserved for the most serious cases. Vaccinia immune globulin, as well as vaccinia vaccine, is made available by the Centers for Disease Control and Prevention (CDC) through state health departments. Consultative assistance in the diagnosis and management of patients with complications can be obtained through state health departments.

Decontamination

Vaccinia virus, if released as an aerosol and not exposed to UV light, may persist for as long as 24 hours or somewhat longer under favorable conditions. It is believed that variola virus would exhibit similar properties. However, by the time patients had become ill and it had been determined that an aerosol release of smallpox virus had occurred, there would be no viable smallpox virus in the environment. Vaccinia virus, if released as an aerosol, is almost completely destroyed within 6 hours in an atmosphere of high temperature (31Â°C-33Â°C) and humidity (80%) (see Table 2 in the original guideline document). In cooler temperatures (10Â°C-11Â°C) and lower humidity (20%), nearly two thirds of a vaccinia aerosol survives for as long as 24 hours. It is believed that variola would behave similarly.

The occurrence of smallpox infection among personnel who handled laundry from infected patients is well documented and it is believed that virus in such material remains viable for extended periods. Thus, special precautions need to be taken to ensure that all bedding and clothing of smallpox patients is autoclaved or laundered in hot water to which bleach has been added. Disinfectants that are used for standard hospital infection control, such as hypochlorite and quaternary ammonia, are effective for cleaning surfaces possibly contaminated with virus.

See the original guideline document for detailed information regarding the viability of vaccinia virus in scabs.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

Diagnostic and management recommendations in the setting of a biological smallpox attack are consensus recommendations of the Working Group based on the best available evidence (see also "Qualifying Statements" and the "Major Recommendations").

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

- Improved diagnosis, management and containment of smallpox following a bioterrorist attack
- Vaccination administered within 4 days of first exposure has been shown to offer some protection against acquiring infection and significant protection against a fatal outcome

POTENTIAL HARMS

Complications of Smallpox Vaccination

The frequency of complications associated with use of the New York Board of Health strain (the strain used throughout the United States and Canada for vaccine) is the lowest for any established vaccinia virus strain, but the risks are not inconsequential. Data gathered by the Centers for Disease Control and Prevention (CDC) in 1968 include:

- Postvaccinial Encephalitis. Postvaccinial encephalitis occurred at a rate of 1 case per 300,000 vaccinations and was observed only in primary vaccinees; one fourth of these cases were fatal and several had permanent neurological residua. Between 8 and 15 days after vaccination, encephalitic symptoms developed: fever, headache, vomiting, drowsiness, and, sometimes, spastic paralysis, meningitic signs, coma, and convulsions. Cerebrospinal fluid usually showed a pleocytosis. Recovery was either complete or associated with residual paralysis and other central nervous system symptoms and, sometimes, death. There was no treatment.
- Progressive Vaccinia (Vaccinia Gangrenosa). Cases of progressive vaccinia occurred both among primary vaccinees and revaccinees. It was a frequently fatal complication among those with immune deficiency disorders. The vaccinial lesion failed to heal and progressed to involve adjacent skin with necrosis of tissue, spreading to other parts of the skin, to bones, and to viscera. Vaccinia immune globulin was used for this problem. One case in a soldier with acquired immunodeficiency syndrome was successfully treated with vaccinia immune globulin and ribavirin.
- Eczema Vaccinatum. A sometimes serious complication, eczema vaccinatum occurred in some vaccinees and contacts with either active or healed eczema. Vaccinial skin lesions extended to cover all or most of the area once or currently afflicted with eczema. Vaccinia immune globulin (VIG) was therapeutic.
- Generalized Vaccinia. A secondary eruption almost always following primary vaccination, generalized vaccinia resulted from blood-borne dissemination of virus. Lesions emerged between 6 and 9 days after vaccination and were either few in number or generalized. This complication was usually self-limited. In severe cases, VIG was indicated.
- Inadvertent Inoculation. Transmission to close contacts or autoinoculation to sites such as face, eyelid, mouth, and genitalia sometimes occurred. Most lesions healed without incident, although VIG was useful in some cases of periocular implantation.

- Miscellaneous. Many different rashes have been associated with vaccination. Most common are erythema multiforme and variously distributed urticarial, maculopapular, and blotchy erythematous eruptions, which normally clear without therapy.

Subgroups Most Likely to be Harmed:

Groups of persons at special risk of smallpox vaccine complications include:

- Persons with eczema or other significant exfoliative skin conditions
- Patients with leukemia, lymphoma, or generalized malignancy who are receiving therapy with alkylating agents, antimetabolites, radiation, or large doses of corticosteroids
- Patients with human immunodeficiency virus (HIV) infection
- Persons with hereditary immune deficiency disorders
- Pregnant women

Note: Under epidemic circumstances, contraindications will have to be weighed against the grave risks posed by smallpox. If available, vaccinia immune globulin can be administered concomitantly with vaccination to minimize the risk of complications in these persons.

CONTRAINDICATIONS

CONTRAINDICATIONS

Under epidemic circumstances, contraindications will have to be weighed against the grave risks posed by smallpox (see "Major Recommendations"). If available, vaccinia immune globulin can be administered concomitantly with vaccination to minimize the risk of complications in these persons.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

- The assessment and recommendations provided in the original guideline document represent the best professional judgement of the working group based on data and expertise currently available. The conclusions and recommendations need to be regularly reassessed as new information becomes available.
- In many cases, the indication and dosages and other information are not consistent with current approved labeling by the US Food and Drug Administration (FDA). The recommendations on the use of drugs and vaccine for uses not approved by the FDA do not represent the official views of the FDA or of any of the federal agencies whose scientists participated in these discussions. Unlabeled uses of the products recommended are noted in the sections of the original guideline document in which these products are discussed. Where unlabeled uses are indicated, information used as the basis for the recommendation is discussed.

- The views, opinions, assertions, and findings contained within the original guideline document are those of the authors and should not be construed as official US Department of Defense or US Department of Army positions, policies, or decisions unless so designated by other documentation.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Staying Healthy

IOM DOMAIN

Effectiveness
Safety
Timeliness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Henderson DA, Inglesby TV, Bartlett JG, Ascher MS, Eitzen E, Jahrling PB, Hauer J, Layton M, McDade J, Osterholm MT, O'Toole T, Parker G, Perl T, Russell PK, Tonat K. Smallpox as a biological weapon: medical and public health management. Working Group on Civilian Biodefense. JAMA 1999 Jun 9;281(22):2127-37. [51 references] PubMed

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ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

1999 Jun 9 (addendum published 2002)

GUIDELINE DEVELOPER(S)

Center for Biosecurity - Academic Institution

GUIDELINE DEVELOPER COMMENT

Members of the working group were selected by the chairman in consultation with principal agency heads in the Department of Health and Human Services (DHHS) and the US Army Medical Research Institute of Infectious Diseases (USAMRIID). The working group included 21 representatives from staff of major medical centers and research, government, military, public health, and emergency management institutions and agencies, including:

- Center for Civilian Biodefense Strategies, the School of Medicine, and the School of Public Health, Johns Hopkins University
- Viral and Rickettsial Diseases, California Department of Health
- US Army Medical Research Institute of Infectious Diseases
- Office of Emergency Management, New York
- Office of Communicable Disease, New York
- Centers for Disease Control and Prevention
- Acute Disease Epidemiology, Minnesota Department of Health
- Office of Emergency Preparedness, Department of Health and Human Services

SOURCE(S) OF FUNDING

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GUIDELINE COMMITTEE

Working Group on Civilian Biodefense

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

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This is the current release of the guideline.

GUIDELINE AVAILABILITY

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Full text available in:

- HTML Format
- Portable Document Format (PDF)

Print copies of the addended guideline: Available from the American Medical Association (AMA) Press by calling (800)621-8335 or by visiting www.amapress.com. Product Number: OP405502.

AVAILABILITY OF COMPANION DOCUMENTS

None available

PATIENT RESOURCES

None available

NGC STATUS

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